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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/117,246	12/03/1998	DOLORES LUDEVID	50062/004001	3466

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BOSTON, MA 02110

EXAMINER

KALLIS, RUSSELL

ART UNIT PAPER NUMBER

1638

DATE MAILED: 04/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/117,246	LUDEVID ET AL.	
	Examiner	Art Unit	
	Russell Kallis	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 January 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3,23 and 42-82 is/are pending in the application.
- 4a) Of the above claim(s) 51,56,65-68 and 76 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 23 and 64 is/are allowed.
- 6) ☒ Claim(s) 1-3,42,43,47-50,52-55,57-63,69-75 and 77-84 is/are rejected.
- 7) ☒ Claim(s) 44-46 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 27 July 1998 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>4/2/99</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I in Paper No. 1/26/2004 is acknowledged.

Claims 24-27 are cancelled. Claims 1-3, 23, 42-50, 52-55, 57-64, 69-75 and 77-82 are examined. Claims 51, 56, 65-68 and 76 are withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 47-50, 52-63, 69-75 and 77-84 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant broadly claims an oligonucleotide comprising a concatenation coding for (P-K)_n wherein 'n' is 2 or more, or a concatenation coding for (P-K) or K-(P-K)₄ or 2K(P-K)₄ either with or without intervening amino acids other than P or K; any plant reserve protein comprising modifications thereof; any maize reserve protein comprising modifications thereof; any maize zein protein comprising modifications thereof; any maize gamma zein protein comprising modifications thereof; and any maize gamma zein preserve protein comprising modifications thereof wherein the oligonucleotide is inserted in place of or following a Pro-X domain naturally present in the gamma zein protein.

Applicant describes polynucleotides encoding 28kDa gamma zein from maize comprising high lysine modifications as P20γZ (SEQ ID NO: 11) having K-(P-K)₄ (SEQ ID NO: 3) inserted after the Pto-X domain, H30γZ (SEQ ID NO: 7) having K-(P-K)₄ (SEQ ID NO: 3) replacing the Pro-X domain, H45γZ (SEQ ID NO: 9) having K-(P-K)₄-E-F-K-(P-K)₄ (SEQ ID NO: 4) replacing the Pro-X domain and pN13γZ having SEQ ID NO: 5 inserted 5 amino acid residues upstream of the carboxy terminus of the peptide (see Figure 3).

Applicant does not describe any other concantenations of P-K in any other plant storage proteins.

The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. The court stated that, "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." *See University of California v. Eli Lilly and Co.*, 119 F.3d 1559; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). Applicants fail to describe a representative number of polynucleotide sequences encoding a plant reserve protein comprising a P-K concantenation falling within the scope of the claimed genus of polynucleotides encoding plant reserve proteins comprising any number of P-K concantenations.

Applicants only describe SEQ ID NO: 6, 8 and 10 encoding SEQ ID NO: 7, 9 and 11. Furthermore, Applicants fail to describe structural features common to members of the claimed genus of polynucleotides encoding plant reserve proteins having P-K concantenations. Hence, Applicants fail to meet either prong of the two-prong test set forth by *Eli Lilly*. Furthermore,

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given the lack of description of the necessary placement of the P-K concantenations, it remains unclear what features identify polynucleotide encoding a reserve protein having P-K concantenations. Since the genus of polynucleotides encoding plant reserve proteins modified to have any number of P-K concantenations has not been described by specific structural features or modification sites, the specification fails to provide an adequate written description to support the breadth of the claims.

Sequences encoding plant reserve proteins having P-K concantenations encompasses naturally occurring allelic variants, mutants, as well as sequences encoding proteins having no known function of which Applicant is not in possession. Accordingly, the specification fails to provide an adequate written description to support the genus of polynucleotides encompassed by the language as set forth in the claims. (See Written Description guidelines published in Federal Register/Vol. 66, No.4/Friday, January 5, 2001/Notices: p.1099-1111).

Claims 47-50, 52-63, 69-75 and 77-84 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for Maize transformed with SEQ ID NO: 6, 8, or 10, does not reasonably provide enablement for any plant transformed and stably expressing any plant reserve protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands*, 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of

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experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

Applicant broadly claims an oligonucleotide comprising a concatenation coding for (P-K)_n wherein 'n' is 2 or more, or a concatenation coding for (P-K) or K-(P-K)₄ or 2K(P-K)₄ either with or without intervening amino acids other than P or K; any plant reserve protein comprising modifications thereof; any maize reserve protein comprising modifications thereof; any maize zein protein comprising modifications thereof; any maize gamma zein protein comprising modifications thereof; any maize gamma zein reserve protein comprising modifications thereof wherein the oligonucleotide is inserted in place of or following a Pro-X domain naturally present in the gamma zein protein; and methods of increasing lysine in plants transformed therewith.

Applicant teaches increased lysine content in maize endosperm transformed with polynucleotides encoding 28kDa gamma zein from maize comprising high lysine modifications as P20γZ (SEQ ID NO: 11) having K-(P-K)₄ (SEQ ID NO: 3) inserted after the Pto-X domain, H30γZ (SEQ ID NO: 7) having K-(P-K)₄ (SEQ ID NO: 3) replacing the Pro-X domain, and H45γZ (SEQ ID NO: 9) having K-(P-K)₄-E-F-K-(P-K)₄ (SEQ ID NO: 4) replacing the Pro-X domain (see pages 27-28 of the specification and Figure 3).

Applicant does not teach any other plants transformed with any other polynucleotides encoding a plant reserve protein having P-K concatenations for increased lysine.

Transformation of plants with non-endogenous reserve proteins either unmodified or modified to have increased lysine introduces an element of unpredictability. The limitation is introduced in finding a host plant that would tolerate the non-native protein and in finding regions that would adequately enable stable expression in a host plant. Thus the screen for adequate non-lethal hosts and stable modified sequences would involve testing many genes and many plants. The inherent unpredictability in stable expression of either an unmodified or a modified reserve protein sequence is illustrated in an example where introduction of either form of a maize alpha zein reserve protein resulted in premature degradation in the seeds of transformed tobacco (Ohanti T. *et al.* Plant Molecular Biology, 1991, Vol. 16; pages 117-128; see Abstract) and in the example where insertion of pN13 γ Z having SEQ ID NO: 5 inserted 5 amino acid residues upstream of the carboxy terminus of the peptide resulted in no accumulation of gamma zein protein in transformed maize (Torrent M *et al.* 1997, Plant Molecular Biology, Vol. 34, pages 139-149; see Abstract and pages 27-28 of the specification).

Based upon Applicant's limited guidance one cannot predict which embodiments would be operable and thus undue trial and error experimentation would be required by one of skill in the art to isolate and test the multitude of non-exemplified plant reserve protein sequences for addition of P-K concatenations to any number of domains for stable expression in a plant, and thus one of skill in the art would be required to screen a myriad of non-exemplified transformed host plants of any species transformed with a myriad of non-exemplified modified plant reserve proteins comprising any number of P-K concatenations in any number of protein domains for non-exemplified expression in seeds in a stable and functional encompassed by the claims.

Given the unpredictability in the art for making DNA sequences encoding modified plant reserve proteins comprising any number of P-K concatenations that would encode stably express in any transformed plant; the breadth of the claims encompassing any plant transformed with any polynucleotide encoding any reserve protein modified to comprise a myriad of P-K concatenations; the lack of guidance in the examples of the specification or in the prior art as to which nucleotide sequences, or domains thereof, would express a stable protein in any host plant or which plants would express the modified gamma zein proteins of the invention; and the undue trial and error experimentation required to practice the claimed invention, the invention is not enabled for the scope set forth in the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3, 42 and 44 are rejected under 35 U.S.C. 102(b) as being anticipated by Coupe *S. et al.* Plant Molecular Biology, 1993, Vol. 23, No. 6, pages 1223-1232 as attached GenBank Accession S42552.

Coupe teaches a proline rich mRNA that accumulates in pod development of oilseed rape encoding a protein sequence [P-K-P-K]-D-P-S-H-K-[P-K]-P-N-[P-K-P-K]-P and thus the reference teaches all the limitations of Claims 1, 3, 42 and 44.

Claims 1-2 and 42-43 are rejected under 35 U.S.C. 102(b) as being anticipated by Forney *et al.* Mol. Cell. Biol. 1988, Vol. 8, No. 1; pages 251-258 as attached GenBank Accession M19784.

Forney teaches a telomere addition in wild type and mutant paramecia that encodes a [P-K]_n wherein n = 10 i.e. [gggttt]₁₀. Thus, the reference teaches all the limitations of Claims 1-2 and 42-43.

Claims 23 and 64 are allowed.

Claims 44-46, otherwise allowable are objected to for being dependent upon a rejected claim.

Claims 1-3, 42-43, 47-50, 52-55, 57-63, 69-75 and 77-84 are rejected.

Claims 23, 45-50, 52-55, 57-64, 69-75 and 77-84 are deemed free of the prior art given the failure of the prior art to teach or reasonably suggest plants transformed with polynucleotides encoding modified reserve proteins comprising concatenations of P-K and expressing said proteins in a stable and functional manner.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Kallis whose telephone number is (571) 272-0798. The examiner can normally be reached on M-F 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Russell Kallis Ph.D.
April 14, 2004

A handwritten signature in black ink, appearing to read "Amy Nelson", is positioned above the typed name and title.

**AMY J. NELSON, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600**